

Activation of the Human Thrombopoietin Gene by Homologous Recombination: Embodiment 1

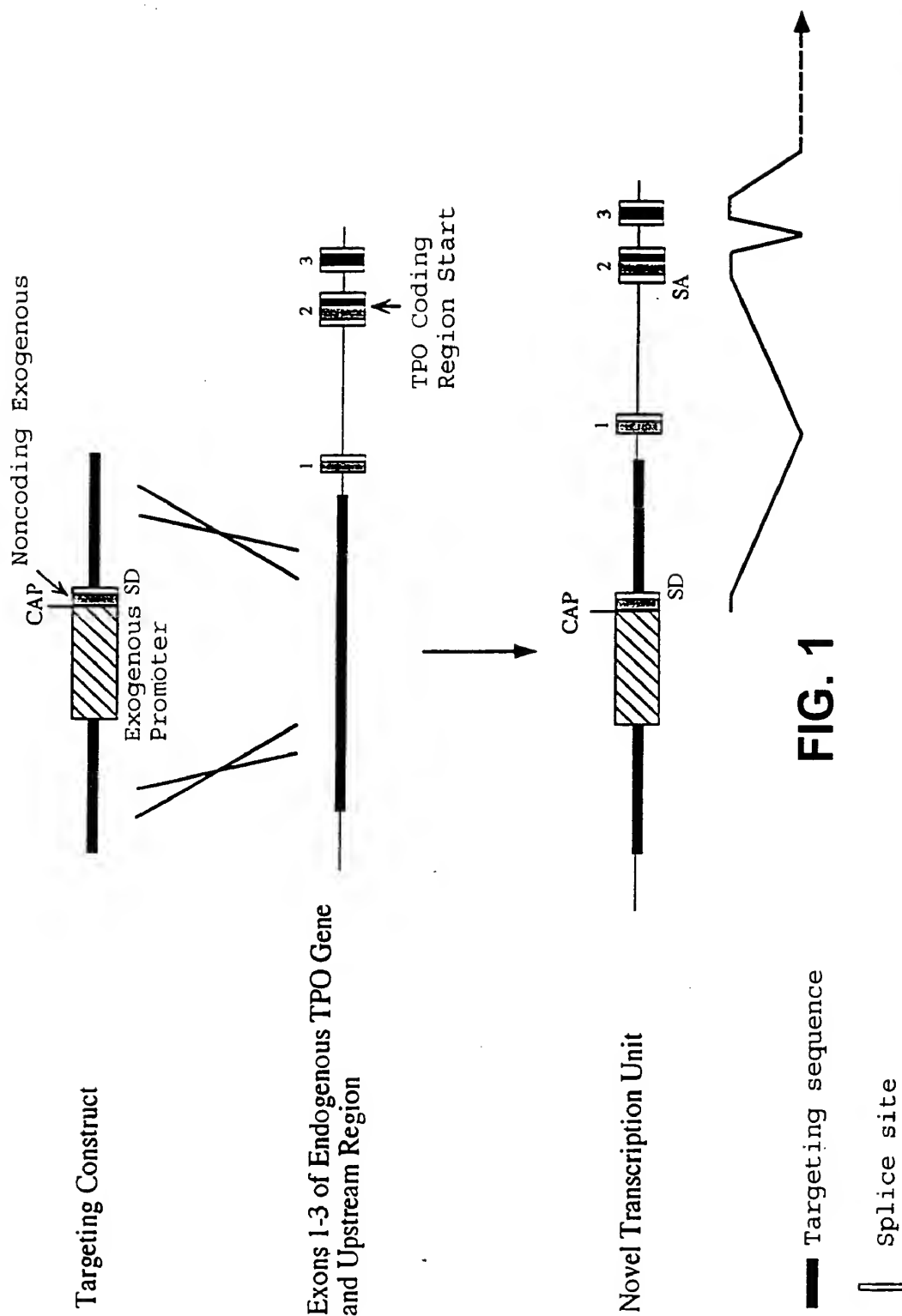


FIG. 1

Activation of the Human Thrombopoietin Gene by Homologous Recombination: Embodiment 2

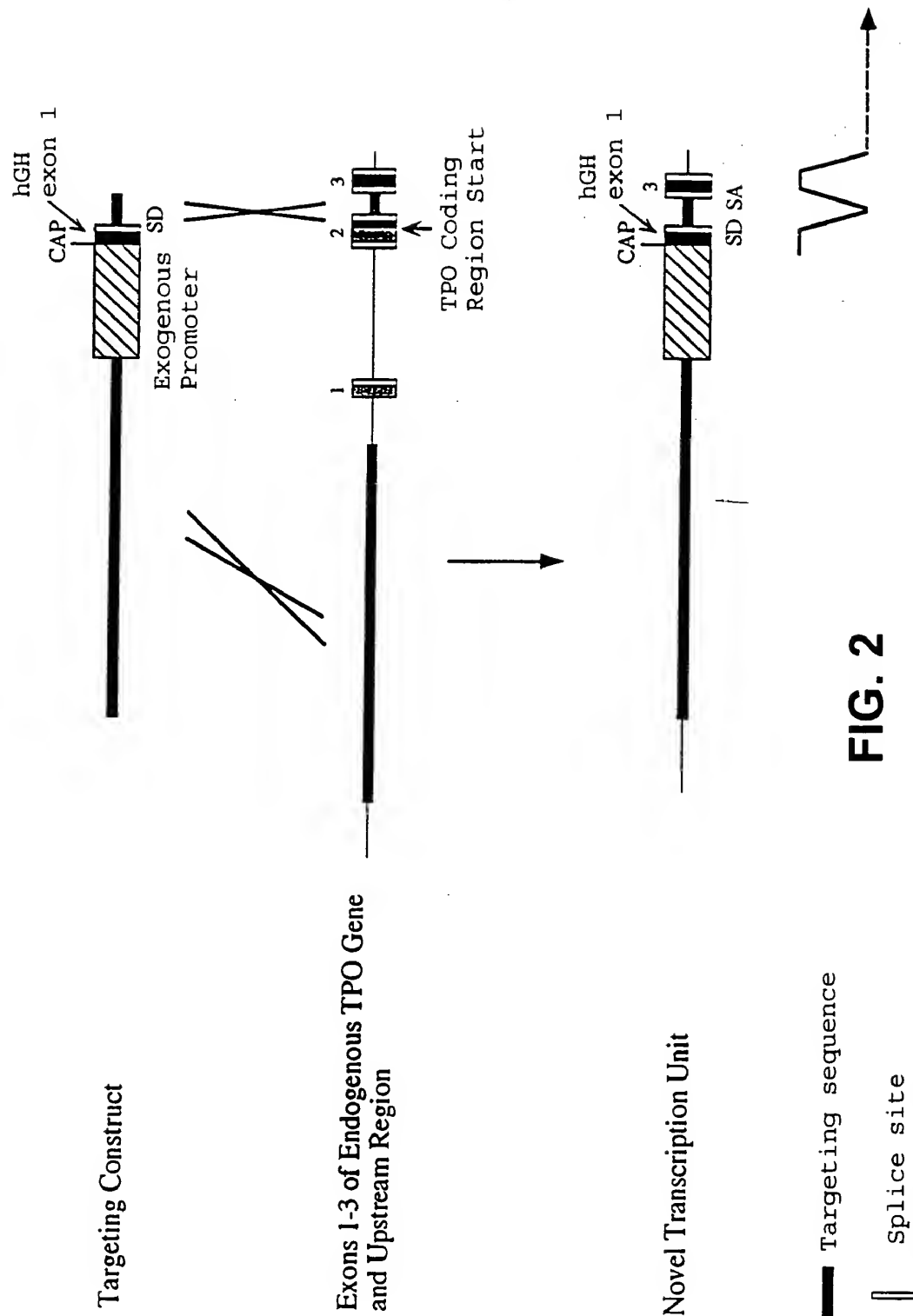
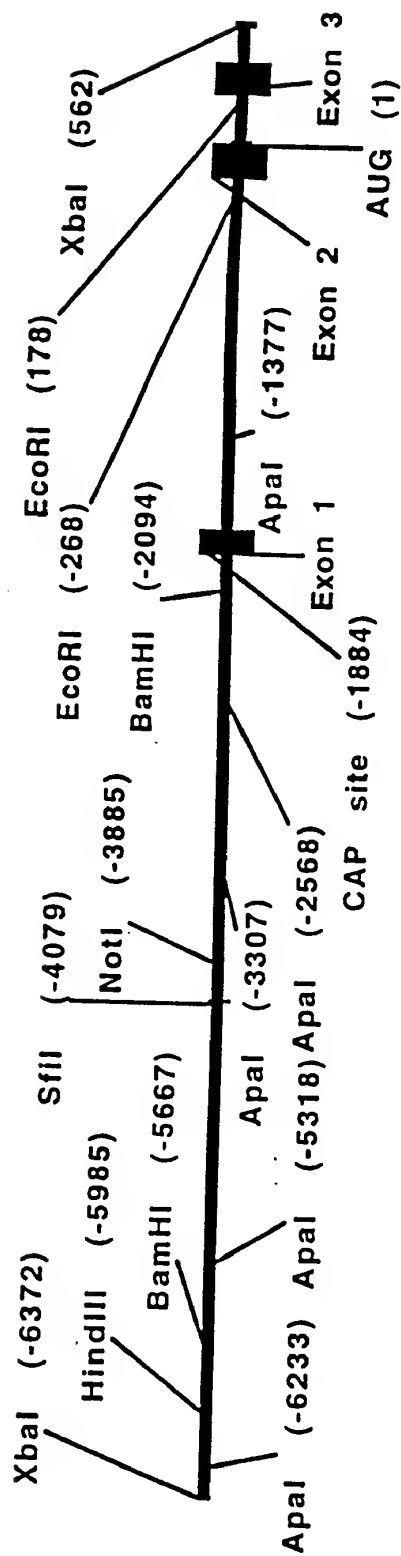


FIG. 2

HUMAN THROMBOPOIETIN

5' Flanking sequence and Exons
1, 2 and 3



425

FIG. 3

665510-212220

XbaI (-6372)

-6373 TCTAGAGTCAGGATGGCACTGAAGGTCTCTGGGGAAGGGACGATGATGAGAGCCCGTCAGAA
-6311 ACCCTCCCCCTTTCTGGGTGATAGAGAAGACTCAGAACTTCACGCCCCGGGGCTCTTTGCT

Apal (-6233)

-6249 CCCTACCTGCAGCCAGGGCCCCGTGCGATGAGAGCCCCCAGACCTCCCTGAAGGGTGAGTGA
-6187 GTGTCACAAGTGCCACATGCAGCTGTTCTGCCCTAAGGAGCCGCAGAGACAACCGAGGCACT
-6125 GCCCCCCACACCCACAGACCTGGAGCAGAGAGACAAGAAGGCCCTACGCTCAGACACTGTG
-6063 CAGGCTAGGCCAATTAGGATGCCCAGGCAGGGCTTATGAAAAGGAACATGGAAAGGAACCT

HindIII (-5985)

-6001 CCAGGGTGCCCTAGGAAGCTTAAGAAAGAACGCTGGAGCCAGATGCTTGGGTTCCAATCCTG
-5939 GCTGCACCACTTCCTAGCTGTGTGACCTTGAATCAAATCACATTATCCTACTGAGCCTCAGT
-5877 TCCCCCTTCTGTAAAAATGGGCATCATAATGTCAGTGCCTTCTCCCACTGGGCTGTGGTGAG
-5815 GACCACGGGAGGCAATGCAGAGCATGCTCTCGGCACAGTGCCCACTGGGCAAGTGCTATA
-5753 AATGGCATCATCTCACCAGGCCTATCTTGGGTTGRGTGGGCTGCAGGGTGCTCAAACAGGAC

BamHI (-5667)

-5691 ACTGCCATTGGAGTCTGAGAAGCGGATCCTGGTAGGGCGGTCCAGCCTGGGAATGAGAGGTC
-5629 GGGTGAGGCCGGACTGAGCCAAAAGCAGCCCCCTCCAGCTCTCCAGTTTCCCTCCSGGCCC
-5567 CGGCAGCGTGACCCCTCCTTGCTCCTTCCCCCTTCTCACCGCCTGTAGGAGATAGAGAAGCG
-5505 GAGGCTAGAGCGCCAGCAGCGAGACTCGGCTCGTGCCACCGCCTGCGACCTCGGCCCTGTCA
-5443 GCAGCGCCACGAAGTCTGGGACGGGAGGAAGATGGCCTGAGCACTGTCAAACGCCGCTTTGG
-5381 TGGCCCAGCCTCAACCACAACCCCGCTGTTGCGCCAGCCCCCTACCCGTGTGGCCGTCAACCAC

Apal (-5318)

-5319 GGGCCCGCTCCTCAGCGCCTGGCTCCCCGCGGTGCTATAACTGCGATGCTCCGGGTCCCGC
-5257 GGATACACGAAGGACAGGCCGCTCGGCTGCCGCTCCGAAGTCTGCGCTCTGCGSGGGGGG
-5195 GTAAGAACACGGGCTTCAGCTGGCCATGGGAAAGGCCAGTCCGACGCCCCATCCAAGTGGCC

FIG. 4A

-5133 CGGGACCTAGTATCGTGGCCCTGCCTCCCTCCCCGCAGCGGAGCAAGACTTACCCTGGGGGC

-5071 AGGTCTGGCAGCAGTGTCCCGGCAGCTGGCGCGGCTGCCCCACAGGCCGGGGTTGGGCACTCT

-5009 GGTTTGATGTTCTTGCAGCTGACCCTGCCAGGCCCTGGTACGGCGACCCCACTGAGGCTGC

-4947 TCCCGGAAAAGGCGGGAAACCAAGTGAGTGCAAGATGCCAACTGATGAGACCCCCCAGGC

-4885 AAGGATGTCCCGCAGAGTCAGCCAGCTCTGCCACTTACAAGCTGCGTGACCCTAGACAAGCT

-4823 ACTTCATCTCTCTGGGCCTCAAGGTCCCTGTCTGGAAAATGGGGATAATAATACTCTCTATC

-4761 TAGCAAGGCTGCCATGAGAGTTAGATGAGCAGGGAACGAAACGGAGTTGGCACAGAGCCTCA

-4699 CACAGAGTGGGCGATCAGTAACAGCACCTAAGAATTGGAGGGGCTGATTCCCTTCTCTCCAC

-4637 CAGAAAAATATCCCCAACATCTGCCGACTGGGCTCCTTCTCAGCAGCTCCGAGTCCACTCCG

-4575 ACGCCCGCGCGACCCGGCCGTCCCCACCCGCCAGCCCGGGCCGGCCGGGGTGCACCTCACC

-4513 GCCTCGCAGGCCACAGCACGCAGCGCATCACCCGAATGGCTCCCTAGGTCCGGGTGCCAC

-4451 GTCTCGTCCAAGGCATAGACCTTCCCGCCGAAGTGCAGCCTGCGGGACGGGCTTGGCTGGAG

-4389 GCGCTGCCCAGCTCGCGCCGTGTGCCGCCCCGGGGGCTGCCCGCGGGTCCCGGGTCCCAGGC

-4327 ACCGCGCCCTTCTGCCCCCGCCACCTTCCGGGCGCCCGCCGCGCCGAGCCACCTGCGCCC

-4265 CGCGCCCCCTCCTCCGGCTCGGCTGACTCGCCCCGAGCCCGACTCCCCGCCCCGCTCCCCCGG

-4203 GCGCCACCTACCCTGCTGCCCCAACGGGCAGCGGCTCCTTCTCAGAACGGATGGGCAGCAC

Sfil (-4079)

-4141 GGGGGCTCTCGGGCCGCGGGGGCGGGAGCCGAGCAGCAGCAGCCCGAGGAGCAGCAGCGGG

-4079 GCCGGCGGGGCCGGGAGGGCHCGGCATGACCGGAACGGGACAGCTGGGGAGGAGGGAGGGAG

-4017 GAGGGCGCGGGAGCGGGCGGAGGGAGGGAGGGCGGGAGTGCGGAGGGCGGAGGGCCGGGCCGG

-3955 GGGCGGTGCGGCGGGAGGGGGCCGGGGCCGGGGCCGGGGCCGGGGCAGTGCCCGCGAGGGGC

FIG. 4B

NotI (-3885)

-3893 TCGTCGGGCGGCGCAGAGTCGGCGCCGGGCCGGGCGGGGAGGAGCGGCGGGAGGAG
-3831 CGCGGGCGGGCGGGCGCTGACCCGGGCGGTACGCGGCTCTACTGCCCCGGGCGCCGGCTCCG
-3769 GCCCCGTTTTATGCCCCGCGCCGACGCCCCGGCGGGGGCCTCCTCCTCAGCAAACGGGGCG
-3707 GCGGCGGCGGCTCGGCGAGGGGCGGCTGAGCCCCGGGGGTCCGACCCAGCAGCAGCGGCCCG
-3645 GATCGCGGGTGGGGGAGGGGAGGGAGGGCTGGGACCGGCAGGGGAGGAGGGAGGGGCGGGA
-3583 GGGGAAGGGGAGCGGGGGAGGGGGAGGGGAGGGACCAGGGGGCGCGAAGAGGGGGAGGAGA
-3521 GGCGGCCCCGA.GCCCCCGCTGCTGGCGGCCACAGGGCGGCTGGACCAGGAGGTCCGTGTCCA
-3459 GCCCAGGAAGGGAGCCTCAGGCTAGGGAGGGGCAGAGGCTTACCTGAGGCCTGGACCGCTCT
-3397 GTGAGCGAGGCCCGGTTCCGCCCCAAGGATAAACTTGTCTTTAAAGATACACGTACAGGAAA

Apal (-3307)

-3335 GGTCCATCAGCCGATCTCCCCCTGCCTGGGCCCACAGCGCCCCCAAACCCTCACCACCCTC
-3273 TCTCACTGCCTAGCCTGCCTCCCTACCTTCTCTCTGAGGTGCTCCTCWTTCCTTGTGTTACC
-3211 CAGRACAGGGACCTAGCCAGAAACCGGCAGCATTCCCCCTTCTGTGGAGTGACAGTATCTCC
-3149 CTCTCATTGTAACCTATCCTCAGGCGCATTGACAGTCCCCCTCTTGCTTTCTCACCCCCCTC
-3087 CTTACCCAAGGGACCCTCTGCCTCTCCAGCCCACTCCCAGCCTCCTTTCTCTTGGTTCCCT
-3025 GGTCAATGCCTGCCTCCCTGTCTCCTGTCTCTCCCTCCACACACCCCACTATCCTCCCAGC
-2963 TATCCCAGCACCCCTCCTTCCTAATCTTGGGAGACATCTCGTCTGGCTGGACGGGAAAATTCC
-2901 AGGATCTAGGCCACACTTCTCAGCAGACATGCCCATCCTTGGGGAGGAGGAACAGGAGAGAG
-2839 CCTGAGGAAGTTCTGGGGGACAGGGGGATGATGGGATCAAGGTCAGGCCAGGAAGCCCCTGA
-2777 GGACAGAGACTGTGGGGAGACTTGGGACTGGGAAGAAAGCAAAGGAGCTAGAGCCAGGGCCA
-2715 AAGGAAAAGGGGGGCCAGCAGGGWGGTATTTGCGGGGGAGGTCCAGCAGCTGTCTTTCCTAA

FIG. 4C

-2653 GACAGGGACACATGGGCCTGGTTATTCTCTTGTACATGTGGAACGGTAGGAGATGGAAGA

Apal (-2568)

-2591 CGGAGACAGAACAAGCAAAGGAGGGCCCTGGGCACAGAGGTCTGTGTGTGTAGCCATCTAAG

-2529 CCACTGGACCCAGCAGACGAGCACCTAAGCTCAGGCTTAACCAGTGCACGTGTGCGCACAT

-2467 ACTGTGCCCCGCACCTGACGTCCACTCAACCCGTCCAAACCCCTTCCCCATAACACCAACCC

-2405 ATAACAGGAGATTTCTCTCATGTGGGCAATATCCGTGTTCCCACTTCGAAAGGGGGAATGAC

-2343 AAGATAGGACTCCCTAGGGGATTACAGAAAGAAAAGCAGGAAAGCAAGCATCCTGTTGGATT

-2281 TCAGCAGCAGGTATGATGTCCAGGGAAAAGAAATTTGGATAGCCAGGGAGTGAAAACCCAC

-2219 CAATCTTAAACAAGACCTCTGTGCTTCTTCCCCAGCAACACAAATGTCCTGCCAGATTCTCTC

-2157 CTGGAAAAAATTCTGCTCCTGTCCCCCTCCAGGTCCAGGTTGCCCATGTCCAGGAAAAGAT

BamHI (-2094)

-2095 GGATCCCCCTCATCCAAATCTTCTCCGTGTGTGCTGTGGGTGGAGTGAGTRGWARCCCTGGT

-2033 CCAGGCAGGGVGCTCCAGGGAAGAGCAAGGCGTCACTTCCGGGSGCCTTCACCAAGTGTCTGG

-1971 TGGCTCCCTTCTCTGATTGGGCAGAAGTGGCCAGGCAGAGCGTATGACCTGCTGCTGTGGA

-1909 GGGGCTGTGCCCCACCGCCACATG

FIG. 4D

Activation of the Human Thrombopoietin Gene by Homologous Recombination with pRTPO1

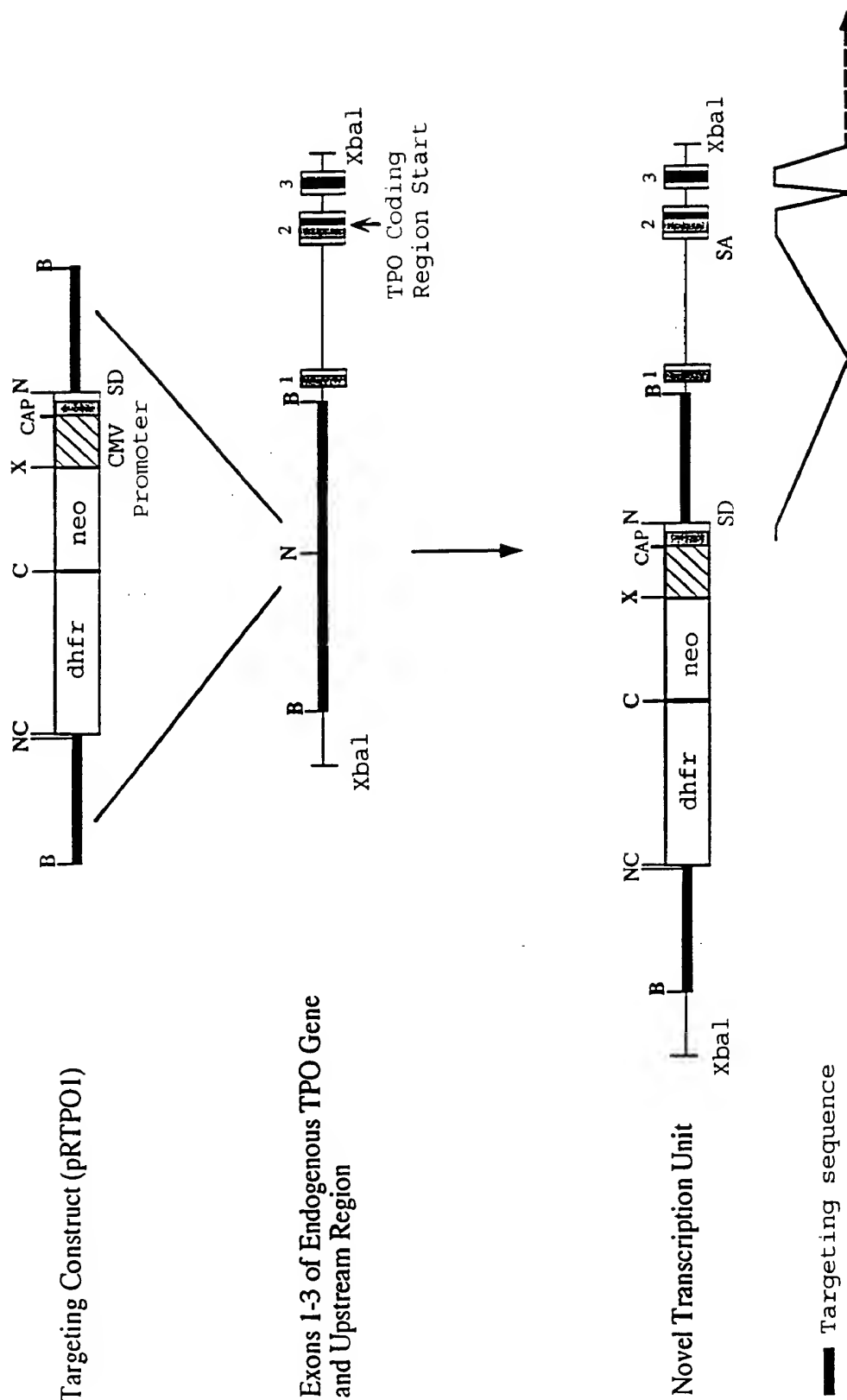
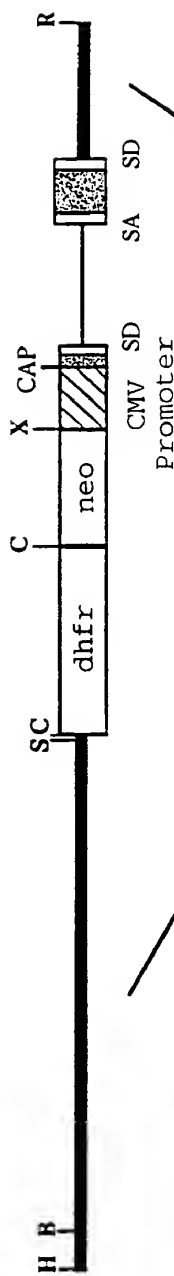


FIG. 6

Activation of the Human Thrombopoietin Gene by Homologous Recombination with pRTPO2

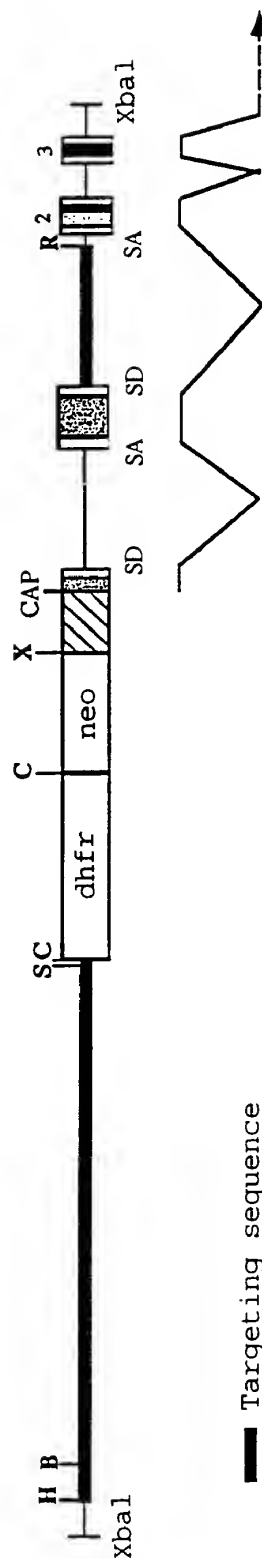
Targeting Construct (pRTPO2)



Exons 1-3 of Endogenous TPO Gene and Upstream Region



Novel Transcription Unit



Targeting sequence

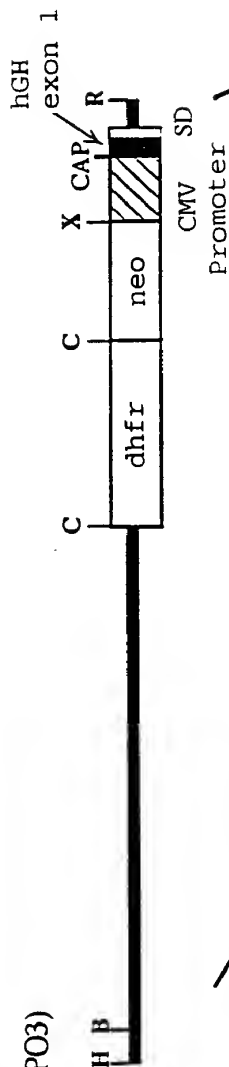
Splice site

= 1kb

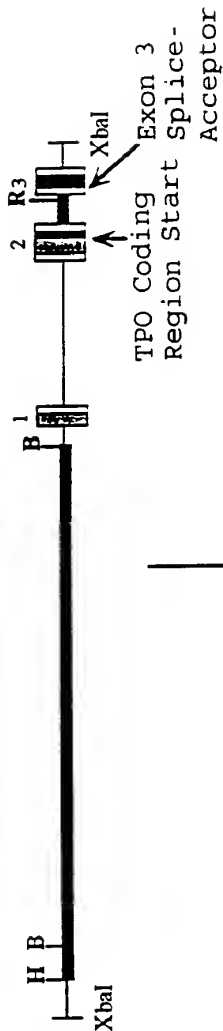
FIG. 7

Activation of the Human Thrombopoietin Gene by Homologous Recombination with pRTPO3

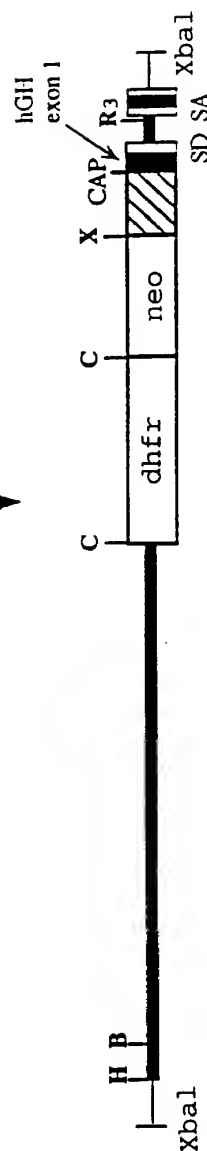
Targeting Construct (pRTPO3)



Exons 1-3 of Endogenous TPO Gene and Upstream Region



Novel Transcription Unit



Targeting sequence

Splice site

=1kb

FIG. 8

Restriction Map of the DNase I 5' Flanking Region Including Exons 1 and 2

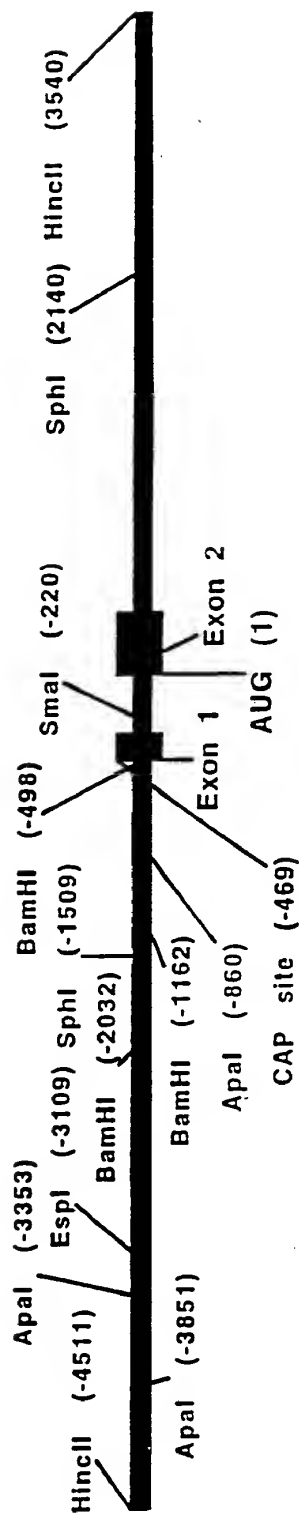


FIG. 9

HincII (-4511)

-4512 GTCAACCTTCACAGTAATTGCTTGTTTCAGTGACTGCCACAACCCAGCCTGGCAGAGAGAGGGAA

-4448 GATACCCTATAAAGCAAGGTAACGTTAATGTTGAGACCATGAATGGCCTTGAGCAGAGCAGAGT

-4384 ATCATTGCTTCCTTCAAATTCAGAAGGATCTGATGGTGCTCTGTGAGTTCATGGGGGTGCCTC

-4320 CGTGCAGGTTGAAACCACAGCTGTCGTCCTTCCGCTTTCCCTCTTGATCAGTAGAAGGGTACCC

-4256 TCCCTGGCCTGCACGTGCTGGGTCAACAACACTGGCTGTCGTTGCACAAAGCCACGGCCACC

-4192 AGCGTTCCTTTGAGGCCATTTGTTTCCAGCCATGGTGCCTATAGGATTTTTCTTTATCCTGTA

-4128 ATTTTCAGCCAAATCAGAGCATGTGACCTGGCTTAGATGTCAATATAATTGTTGTTATGTGCTCT

-4064 TTTCCCTTCCTGTGTCTGTGACAGGTTTAATTTAACCTGAGAAGGCTGCAGATCCTCGGGGGTT

-4000 GGTGTAAAAACACCTCATCCTGATCTGAGAAGGCGGTCAGCTTTTCTCCTCGTTGCCGTTGGCT

-3936 GCCAGCACCCATTCTCTGTGGATGTGAAAATCCAGAAGGGCTGGGCTTCCTTCTTGGCATTCC

Apal (-3851)

-3872 CCAGGCCTATCTCCAGAGTGGGGCCAGCATGGGAGGATTGTACCCCACTCACTCCCCCTGATGT

-3808 GGGGCTTGACCTACAGCTCGACAGCACCCATGGAATGTGGGCAGAAGCGACAGCAGCCAACGT

-3744 CCGCCTTGCCCTTAGGGCGGCACGTGTTCTGCTTGTGCCCTGGGAGCCTCCACCTTCCCACTG

-3680 TGGGAAGAGGGTGCCAGGGAGCTGCAGTCTCTCCAGCCCAGCCCCAGGACGAGGCCAGGCAG

-3616 CAGAGCCACCCAGCAGACCTGGCAGTGTGAGAGAAATGCATGTGTATACACTGAGTTTGCAGG

-3552 TGGCTGTTACATGGCAGCATTGACTGACACAGACAGAAAAGAGATCCACGAGGGAGAAGTGAGA

-3488 GTGCTGGAGACTCCAACAAGCCACAGGCTGCAGGGGCAGGATGGCTTCTTAGAAGGTGAATGAT

-3424 TGTTCTGGGAATCTATCAGAGGAAGACATAGAGGCTCCAGACGGTTGAAGGCCCAACAGTGATC

Apal (-3353)

-3360 CCAGACGGGCCCCATGTCAGACCAGGCTCCTCCAGGGCTGTCGCTGCCCTCACCAAAGCCCGTC

-3296 CTGAGGGCAGCCACACAGCAGGCAGCACTCGCCATTTGTACAAGCGAGGCCCAAGTTCCAGCCT

FIG. 10A

-3232 TCCTTCTGGCAGGTAGAGGAAGCAGGGGCACTATGCCTGGGAGTTCTTGAAAGCAGATGGGGCA

-3168 GCATTGTGGTCAAGAGCCAGGAGGGGATGACAGACCAGAGGGGAACCCCTCGTCCACGTGCTGAG EspI (-3109)

-3104 CACACGTAGGGGGTTGGGCACTTGCTCTGTGAGCTATAATTGGTGTCCCTGTGCCCCGCCGAA

-3040 GCTGCACCAGGCAGTTTCTTGGTGGAGGACAGTGGCCGCCCTCTAGCTTTACTCCCTTCCCCGT

-2976 GATGGGTCGCTGTCAGATGTGTGTCCAGGAAAGGCAAACACCAAAGGCAGAGGACTAGTCCCTA

-2912 CACCGAATACTCCGGTGGCCTTGCTTGGGGGCTGGGTTTTGACGTGCTGGAGGCTGTCCCTAGAC

-2848 TTAGAGATTAAAAACAGGGAAGAACCATTGCTGAAACCTTTGGAAAAGCCTGCAATGGCCTCTG

-2784 GCAGCCTGAGGAGTGGTGGTGTTCATCTGGTAGACGCCGTCTCAATAGGAGGGACAGATGAG

-2720 TGCACCAGTGCTGCCAGCCAGAGGCGTCTGTTGGCGTGTCTTTATGGAATGGGGTGCCAGTCTT

-2656 GTGGAGGGTGGTTTTACCTTCCTGTTTTCTAGTCCCCACTGGGCCTGCCTTCTGCTTCATGCCAGC

-2592 TGGCCAGACCGAGCACTTTCCTGACTTTCGACCTTGGCCCCCTGCTGACTCTTGCCGTTGAGGCC

-2528 TCCTGCAGACCCCATTTGTATTCAATTCCTGCAGTTCTCATACCTGAATCCCGCCTGGACTTCT

-2464 GCCAACCGTTCCAGGCCCTCCTCCCAGGGGACCACAGATGCTACGTGCAGGGCTGTCCCTTGA

-2400 GGGCCAGCACAGCCCCCTTCCAAGTGGGCAAGACCCAGGGGTGGCTCAAAAGATAGCTGTGCCCT

-2336 AGCCCTGGAACCTCTGAATGTTGATTTTTGTAGCAAAAAGGACTTGCAGATGTGAGTAAAGGC

-2272 TGTTGAGATAAGGACATCCTCCCTGCTCTCTGGGAGGACCCCAAATGCAGGTGCACAGATCTTA

-2208 AGAAGAAGAGGCAGAGACTGGGGTGATGCAGCCACAATAAGGAAAGCCAAGGATTGCTGGCAG

-2144 CCTGCAGAAACTGGAGGGCAAGGAGCATCCCCCAACCGCCCGGAGCCTCCAGGAGGCGCAAGGT

-2080 CCTACTGACTCCCTGACTTCAGACGTCCAGTCTCCGGAATTTTGAGAGGATCCATTTCTGTTAT BamHI (-2032)

-2016 TTTAAGCAACCAAACCTGTGGTAGTTTCACCAGTCTCAGGAAATGAATACGAATGGAAAGTCAA

FIG. 10B

-1952 AGATTCCAAGAAATGAGTGGCGGGGTGCGGTGGCTCACACTTGTAAATCCAGCATTTCGCGGGAA

-1888 GATTGCTTGGGCTCAGGACTTGGAGACCTTGTGTCTGTGAGAACTTAAAAAATAGGCTGGGTG

-1824 CGATCGTCACGCCTGTAATCCAGCACTTTGGGAGGCCGAGGCAGGCGGATCACAAGGTCACGA

-1760 GTTTGAGACCAGTGTGACCAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAAATTAGCCG

-1696 GGTGTGGTGGTGCCTGTAATCCAGCTACTCGGGAGGCTGAGGCAGAAGAATTGCTTGAA

-1632 CCCAGGAAGCAGAGGTTGCAGTGAGCCGAGATAGTATTACTGCACTCCAGGCTGGGCAGCAGAG

SphI (-1509)

-1568 CAAGATTCCGCCTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAACTGAGCATGGTAGCATGC

-1504 ACCTGTGGTCTCTCGTACGCCGGAGGATTGCCTGAAGCCAGGAGTTCAAGACCAGTCTGGACAAA

-1440 AGAGCAAGACCCCATCTCTACCAAAAAAATTTAAAAATTAGCCAGGCATGGTGCCGTACCCATA

-1376 GTCTTAGCTACTCAGGAGGCTGAGGAGGGAGGATTATCTGAGCCTGGCGGTTGAGGCTATAATG

-1312 AGCCATGATTTGGCCACTGCACTCCAGCCTTGGCAACACAGTGTGAGACCCTGTCTCAAAAACA

-1248 ATAAAAACCCAAAACAAAAGAACCAAGAAATTACTGGACCTGAGCCTGGCCTTTAGCTGCTGCC

BamHI (-1162)

-1184 CTGCCCTKTGACTGGTCACTCGGATCCCTGGGCCTAAACACACAGCCTATTGTCTACCTCAAGA

-1120 AGGCTCCCCACTGCTTGGCTGGCAATTGGGGTGGCTTTGCAGGCCCCACCTGTCCTGGCCCCAC

-1056 GGCCTGGTGCTGCAGGCCCCCACCCTGCTTGTTCGAGCTCCCAGCCTCCTGCAGAGTTGC

-992 CTGCACCTGATGGCGATGAATCAGGAAGGCAGGCGTGTCTGGGCCACAGAGCAGTCATGCTGT

-928 CAGCCACCAGGGGGCTCCATTTGCAACTTTGGATGTGGCTTTGGCCTCTTTGTCCAAAGTGACC

ApaI (-860)

-864 TTGGGGCCCCCAGACAAGAGACAGGGAGACTGGAGCCCAGCCCCACCCTCCCGCACATACCTGG

-800 CCCATCCCTGCCCTATCCTGGAAGATGGGGGCCACCACACGTRCAAGGGACACGGGATAGGAAC

-736 CTTTGGCCTTGTATCAGACATTTTAAACTAAGTGCAAACGTGATTATCAGGTGCAGTTTTTA

FIG. 10C

[illegible]

-408 AGGAGAAAATTGTCATCAAAGGATATTCCAGATTCTTGACAGCATTTCTCGTTCATCTCTGAGG

-284 GCAGGGAGGGAGGCTTAGAGTCTCATCCTCCAGCAGCGAGTGAGGCGGAGGCTCCAGCGTCC

-222 TCCCGGGCGGGTTTCTGGTGGATGGAGGAGTGACTCGGGGTCTCTACGTGGTGCCAGCTG

-98 CCACCAGCCCCTGCCAGCTGGGCTCCAGAAGGCTGGAGTGCTGTGGCAGGGATGACGTCTCA

-36 CTTCTGTTATGTCTCTGTGCCCTGTGCTCTCCCAGG ATG AGG GGC ATG AAG CTG

64 TCC CTG AAG ATC GCA GCC TTC AAC ATC CAG ACA TTT GGG GAG ACC

109 AAG ATG TCC AAT GCC ACC CTC GTC AGC TAC ATT GTG CAG ATC CTG

154 AGC CGC TAT GAC ATC GCC CTG GTC CAG GAG GTC AGA GAC AGC CAC

199 CTG ACT GCC GTG GGG AAG CTG CTG GAC AAC CTC AAT CAG GAT GCA

244 CCA GAC ACC TAT CAC TAC GTG GTC AGT GAG CCA CAG GGA CGG AAC

289 AGC TAT AAG GAG CGC TAC CTG TTC GTG TAC AGG CCT GAC CAG GTG

334 TCT GCG G

FIG. 11

Activation of the Human DNase I Gene by Homologous Recombination with pDNase1

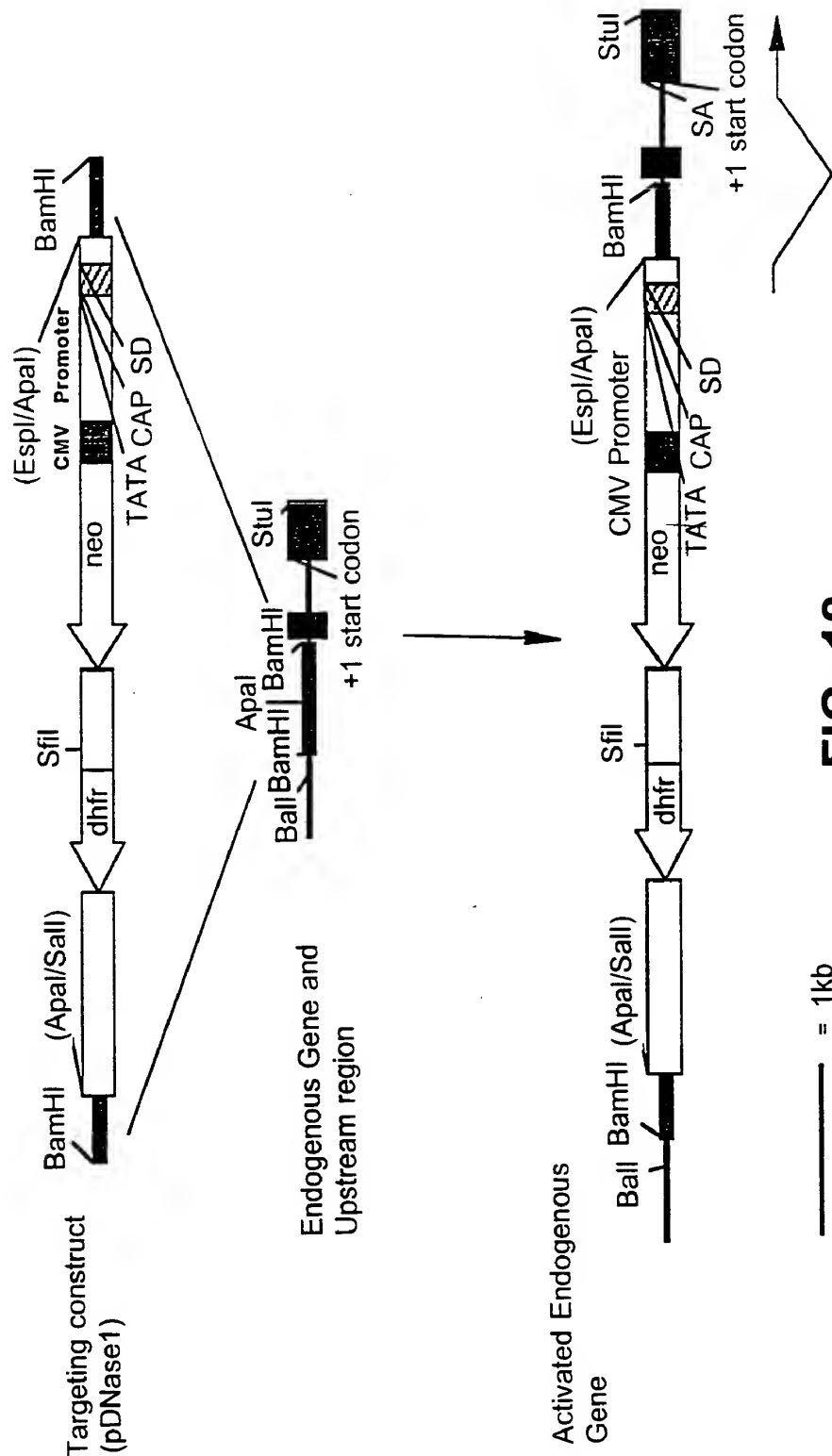
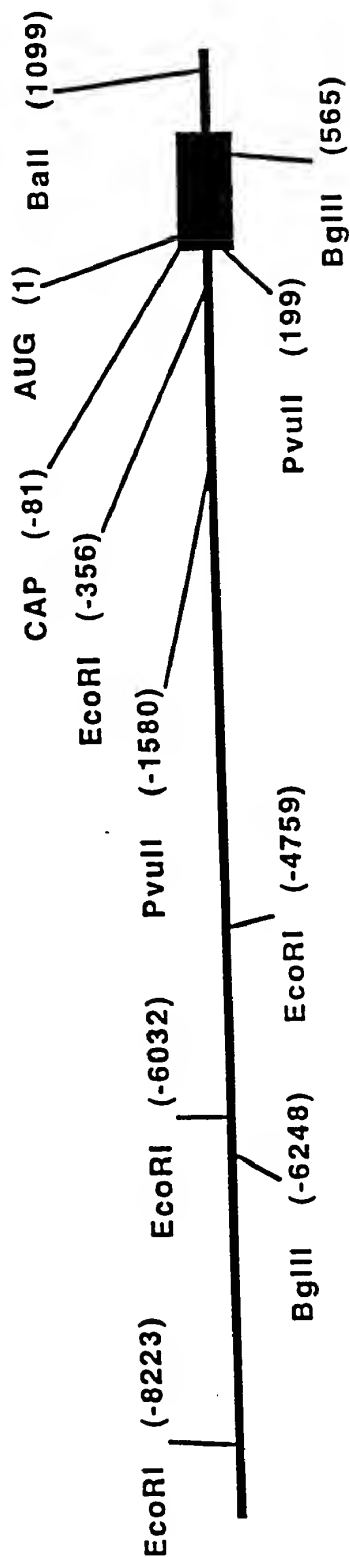


FIG. 12

Human β -Interferon

5' Flanking sequence,
coding sequence and 3'
untranslated sequence



600

FIG. 13

-8711 AGCTTCTGCTTTAGGAAAGTAGAAAAATAAGAGCAAATTAAATCCAAGGTAAGTAAAAAAAAAAAAA
-8646 AAAAAAAAAAAAAAGAAATAAAAATTAGAGCAGAAATCAATAAAATTGAAGACAGTAAATCAATAAA
-8581 GAAATCAACATAAAAAAGTCTGGTTCTTGAAAAGATATATAAAATTGATAAGCATCTACCTAGGA
-8516 TAATTAAGGAAAAAAGACAGAGGACACAGATTACTAATATCAAACATAAAAGCGGGAACATCACT
-8451 GCAAATTTTATAGGCATTGAAAAGCGTAATAAAAGAATACTATAAACTATTCTATAACTACAAATT
-8386 TGATAAGTAAATAGAATGAACCAATTCCTTGAAAGACATAATCTGAAAAATGTAAAAAGAAGAAA
-8321 TAAACAATCTGAATAGCCTATATCTATTAAATAAAATTGAATCAGTAATTAATAACCTCTCAAAC
-8256 AGGAAGCACAATGCCCAGATGGGTTCAGTAGTGAATTCCTATCAATATTTTAAAGAAAAAAAAAATT
EcoRI (-8223)
-8191 GTATCAACTTTCTACAATCTCTTTTCAGAAGACAGAAGCAGAGGGAATACTTCCTAAATCATTCAA
-8126 CTAGGCCAGCATTACCTTAATACCGGAACTAGAAAAATGACATTACAAGAAAAGAAAACAACAGAC
-8061 CAATATCTCTCATGAACAAAGATACAAACATTTTCAACAAAATATTAGCAAAAAGAATCCAAGAA
-7996 TGTATCAAAAAATATACACCACAACCAAGTAGAATTTTATTCCAGATATGTAAGGGTGGTTCAACG
-7931 TTTGAAAATCAATTAACGTAATTTGTCCCATCAACAGGTTAAAGAAGAAAATCATATGGTCATAT
-7866 TGATAGACACAGAAAAAGCATTGACAAAATTTAACACCCATTTCATGATGCAATCTCTCAGTAAA
-7801 CTAGGAATAGAGGAAAACCTCCTCAGCTTGAATGTACCTTCCTCTCAATTTTGCTATGAACCTGA
-7736 AACTCCTCTTAAAAAATAAAGTTTTTCATTTAAAAAGAAAACAAAAACATGGAGGAGCGTTGAT
-7671 GTATCTCATTTTAGACCAATCAGCTATGGATAGTTAGGCGACAGCACAGATAGCTGCTGTACTTC
-7606 TGTTTCTGGCAATGTTCCAGACTACATTTAAAAAATTTTAAATTATAGACTTGTAATTAATGTTC
-7541 AAGAAAAATATGAAAATGCTTTGCCGTGTTAATGCTACTCTTTTTTAAAAAAACTAAAGTTCAA
-7476 ACTTTATTTATATTTTCATTAGTTTTTTAGCTACTGTTCTTTTTCTGTTCTGGGATCTCATTTCAGA

FIG. 14A

-7411 ATGCCACATTACATATAATTCTCATGTCTCCTTGGGTTCCCTCTTAGTTTTGACAGTTCCTCAGAC
-7346 TTTTCTTATTTTTGATGACCTTGACAGTTTTGAGGAGTACTGGTTAGATATAGGGTAATGGTTTT
-7281 TAAAGTATATTTGTCATGATTTATACTGGGTAAGGGTTTGGGAGGAAGCCATGGGTAAGTACTGT
-7216 TCTCATCACATCATATCAAGTTATATACCATCAATATTGCCACAGATGTTACTTAGCCTTTTAAAT
-7151 ATTTCTCTAATTTAGTGTATATGCAATGATAGTTCTCTGATTTCTGAGATTGAGTTTTCTCATGTG
-7086 TAATGATTATTTAGAGTTTTCTCTTTCATCTGTTCAAATTTTGTCTAGTTTTATTTTTTACTGATT
-7021 TGTAAGACTTCTTTTTTATAATCTGCATATTACAATTCCTTTACTGGGGGTGTTGCAAATATTTT
-6956 CTGTCATTCTATGGCCTGACTTTTTCTTAATGGTTTTTTAATTTTAAAAATAAGTCTTAATATTCA
-6891 TGCAATCTAATTAACAATCTTTTTCTTTGTGGTTAGGACTTTGAGTCATAAGAAATTTTTCTCTAC
-6826 ACTGAAGTCATGATGGCATGCTTCTATATTATTTTCTAAAAGATTTAAAGTTTTGCCTTCTCCAT
-6761 TTAGACTTATAAATCACTGGAATTTTTTTGTGTGTATGGTATGACATATGGGTTCCCTTTTATTT
-6696 TTTACATATAAATATATTTCCCTGTTTTTCTAAAAAAGAAAAAGATCATCATTTTCCCATTTGTAA
-6631 AATGCCATATTTTTTTTCATAGGTCACCTTACATATATCAATGGGTCTGTTTCTGAGCTCTACTCTA
-6566 TTTATCAGCCTCACTGTCTATCCCCACACATCTCATGCTTTGCTCTAAATCTTGATATTTAGTGG
-6501 AACATTCTTTCCCATTTTGTCTTACAAGAATATTTTTGTATTGTCTTTTGGGCTTCTATATACA
-6436 TTTTAGAATGAGGTTGGCAAGTTAACAACAGCTTTTTTGGGGTGAACATATTGACTACAAATTT
-6371 ATGTGAAAAGAAAGTATACCTTCACAATATTAAGTCTTTTAGTTCATGAATATAGTATGTCTCTC
-6306 CGTTTCTGCATTAACTTAGACATTCATTAATTTCTCTCACAATTTATAAGTTTATTTAGATCTTC
-6241 ATTCATTTAAATCTTCACTAACCTCTCATTTACAATTTGTAAGTTTTCTGGGTAACAGTCTTGCA
-6176 CTTCTTTGCCTAGATTTTATTTCCAAGTAGATTATTTTCATACATCGTCTATGGTGTCAATTTTTAA

FIG. 14B

-6111 AATGTAATTTTTCACCTTTTTATTGCTAAAGAGAGATGACTGATTGTTAATATTGATCTTGTGCG

EcoRI (-6032)

-6046 TGGCGACCTTGCTGAATTCTAATCGTTTATCTATAAATTCTTTTGTATTTTGAATGTAAACAATT

-5981 AGATCATCTGCATATAATTTTTAAATCTGATAAGTCAACAAGAGATTGAAACAGGCTCTTCACA

-5916 AAGAAAATATCCAAATGGTCAATAAACATATGAAAAGATGCTGAAACTTGTTAATAATCAGAGAG

-5851 ATGCAAATTAACTATAATGAAGTATTATTGTACAACAATAGAATGACTGAAATTAAAAAGACTG

-5786 ACAATATCAAAGTTGGCAAGAGTCTGATACAACCTGGAATTCTCAAACACTGTTAGTAAGAATGT

-5721 AAATTGGTACAAACATTTGGGAAGTCATTACAATATTATCTGCTAAATCTGAACATATACATATT

-5656 CTATGAGCCAGTTACTTCATTCTAGGCATATACCCAAAAGAAGTATGTACTATTGTGCAGTAAAA

-5591 AATACAGACAAGGAATTTTCATAGGAGCATTAATTATCATGGCAAATATTTTAAAAAATTATTAGT

-5526 AGTAGAAGGGATAAAACATTGTGGTATACTTCTAAATAGGGTAAACACATTAATGTAAATTAAT

-5461 AAACATACACACAAGATAGACGAATTTCCGACACATTCTGTTGAGGGTAAGAAGACCATTTATA

-5396 CAAAGCTCAAAAACAGACAGAATCTAGAGTGTTAAAAGACTGCATGGTAGTGACTTTGGGAGAAG

-5331 AAAGTAGTGACGAGAGAGAGGAGAGAGAATAATGATTGCGAGGTGCTATAGTCTGAAGGTTTGTG

-5266 TCCCCCAAATTTTCACATGTTAAACCTAATCCCCAATGCAATCATTTTAAGAAGTGGGTCCTTTA

-5201 GTGGATAATTAGGTAATGGAACAAGAGCCCTAACAAATGGGATTGGTGCCTTATAAAAGAAGCCT

-5136 GAGCCTGAGGGACCTTGTTTCCGCTTCTACCATATGAGAATGCAATGAGAAGGCACAAAGCAAA

-5071 GAGCAAGCCCTCATCAGACACTGAATCTGCTAGGGCCTTAGTCTTGGCTTTTCCAACCTCCAGAA

-5006 CTATAAAAAGAAATGCTTGTTGTTTAAAAGGCATTTCAGTCTATCGGTGTTTGTAGAGCAGCCC

-4941 CAAGAGACTTAAGAGGGAACAAGAGGGCGATTTCTGTTGTGTGATAATGTTTAGTTTGTGGTTA

-4876 CAAAGAGTGCAGACGTTTTTATTTTATAACAATTCATTGAGCTATATCTTAAGATGTATGCGTAA

FIG. 14C

EcoRI (-4759)

-4811 TTTTCTATGTATATTATTGTTTTATAAACTTTTCTTAAAAGAGGAAATGGGAATTCTCCCTTTT
-4746 ATGTATTAATCTCTTATGAAAGAGTTTGTGGCTTCCCAAGATATTTCTGAAAGATTGCTTTTGG
-4681 CTTCAATTTATGTTCTGCCACTGCTTATGCACCTCTCAATAACTCTTCATCTTGTATAATTTATCA
-4616 TTCTTTGATAGGGACCCCTCTTCCTTGAAAAATAATTGAAGATATAAGGAGGAGGAAGAGAAGACA
-4551 ACTAAATGTTTATTTCTAGATACATAGTAGTCTGCATAGATAATTATATTCAAAGAGGAGGACA
-4486 AATTGGCTCCTATCTCTGAAATTTATAGAAAAGCATTTCACATTAAAGTGATTTCAAATGACTA
-4421 GAAATGTCATTCAAGTTTTACTTTCTAAATGTCACCTCTGTCTCTCCAAACCTCATTAACCACAAG
-4356 GAACTGGTGCAGGGACTGGAAGTAGTTTTCTCATACAACGGAAAGTTAACGAGGGGAGGAAAGGA
-4291 TGTGTGCAAAAATAACGTCCACAGAAGGGACAAATAACAAAGGGAAAGATGACAGGAAAGGGTTC
-4226 GGGCACTAACCCTTACAATGCAGATACACACTGGGCTGGTCTAAGAAATAGGGTTCCCTGGTAGA
-4161 CAGAAGGTTAAATAAATTTTCTGGTTATTCTGATCAACTCTAATAAAAGAAGAGAAATGAAGC
-4096 TAAAACTTAAATGATGTATTTAAAGGAAGAAATTTTAACCCATTTCATAGGTGAGCTTCTGCCA
-4031 AGATTACTACTAATCCTCAGGAGAAGGGGTAGAGGAGAACTCCATAAAGGCAACTGGAAGTGGA
-3966 GTATTAGGAAGCACCTCAAGAACACAATAGCAGGAAGTAGCTAGAGAACAAAGAGAAGAAAACCA
-3901 GAAAAAAAAAATCCCTTTTTATTTTTCTGTTTCCATTCTTTGGCTCCATTTCCACAGCTATGGC
-3836 CTTTATTTTACCCTCCACAGCCATGAGAGCCTCTGGGCAGGAGTTCTCTCGCCTCTCCCTGTT
-3771 CCAATCACCTCTAACATTTCTGCCTATTGTTCTGCCCAGGGAAAAAACTCCAGTCTCTTCTCTGT
-3706 CAAAGACCTCTTGAATTAAGTCCAAATGCTACACTCTGGCATTCAAGACTCGTAATACAGCTCAA
-3641 CCTGACTTTTCCACCCTCAGCCTCCTTGATTCTTAAATGAAGCCTGTCCACAATTGAAGCTCCT
-3576 TGTCTTTGCTCCTGCAAATTTGTTCAATCTCTCTGGCTGTGTTTGTGCTGGTCTCTGTCTATCTAG

FIG. 14D

-3511 AGCTGTGGATATCATGGTATCTATTGTCTATCATGCTAGCCATGAACCACATGTGGCTGGTGAGC
-3446 ATTTTATATGGTACTAGTCTAAATTGACATCTACTGTGAGTGTA AAAATGTGCATTATGTTTTGA
-3381 AGACTGTACACAAAATTTAATTATCTCATGAATAATTTTAGATTGGTTATATGTTGAAATTATAA
-3316 TATTTTGGATATACTATGCTAAATAAAACATATTATTAAAATTAACCTCACCTGTTTCTTTTCCT
-3251 CTTTCAATATGGCTACTAGAGCTTTTAAATTCATTATGTGACTTTATTGGACAGTACCGATTG
-3186 AATGCCCTCAACCACATCACCTCACCCAGCCACCTCTACCTGTAGTGATCATACCACTTCTTTA
-3121 GGCACACTGCCTGCATTAAGGGCAATGAATGCCTTTTCATCTTCTCCACTAGATGTAGTTTCTTT
-3056 TTTCTTTGAGAGCCATCATCACCATCATGGTTGACACCATGAACCTATCTGAAGATGTCAGCCAT
-2991 AGACTGCTTGATATTCTACAGGAAAGATCACAGTTTTAAGTGCAATCTACCCATGTTATTAGCAG
-2926 TGTGTATCTTTCACACATTACACAGCCTCTCTAAGCCTCATTTCTCTCCTCTGTAAGATGGGGAT
-2861 GATAATAACCCATCTCAAATGTTTACTATGAGGATTATTCAAAGAATGGCAAATAGCAAGTGCTT
-2796 AATAAATGATAACTAGTACTACCGCCACTACTGTTGTTTTTATTGTATTAGATTATGAACTCTCT
-2731 AAGGACCATTTCGGGATGGAGGATAAGAGACCATTTGATGTGGGCAGTGATGAGGCCTTCTGTTG
-2666 CACCTGGAAAGGTCAACTATATACAAGCCTGCAAGTCATTCTATAGGAGCAGGCCCCAGTGACCA
-2601 GACTCTATAGACTGTCTCCTCTTTCTGAGAGGGACAGCCATCTCTAGGTTGACTAACCTCTGAA
-2536 GCTCCTTGCAATGGCTTTTGTGCTATGAGCCATGGATGATTCCAGACTAATCCGAGAATGCTCGT
-2471 CAAAACCCCAAGGAATTACTCAAATACTGACATAACAGACATTTTTTGAGTGGAAGAGCCGAGTTT
-2406 TTTTAAATATTCTGAAACTCATTGTTTTTAAAAATGCATGAGATGGCCAAGGTCTTGCTAAGAGCT
-2341 GGCCTGCAAAGCGAAAGGCAGAGAGAATGAAACCCATAGAGAGGCAGAATAACCAGAAAGGTTGG
-2276 GACTCGTTTTATTTTATAATGTAAATTAGTCTATTATGAAACAATACTTGTTTTACTGGTGAAAAAT

FIG. 14E

-2211 TGGAAATACAAAGAATAAAAGGAGGAAAAAATCACTCTTTAGTTTCACAAGCCAAATCAAGCC
 -2146 ACTATTAAAATGGTGGTTTACTTCCTTTTATTAATTTTCTGTACATATTTTGCATAATCATGTT
 -2081 GTATGTACAATTTTATGTTCTATTTTCAATATTAAGTGGTGTCTTCAAATTCCTAATGACAA
 -2016 AAATAATATATGCTCATAATAGAACATTTTAAATGCAAATAAAACAAAAATAATGTTAAAATTTA
 -1951 GTAATATTTATTAAATTTTCTCCAAGTGCACGAAATTACAAATGTAACAACCTAATTCCTAGTG
 -1886 GCCTAATAACCCTATTTCCAGACCTCTTCTCATTACAAGGAAAACTCATATGCAGATAGTTCTA
 -1821 AAGGTATGAAGTGAAAAGATAAAGATTTTCTTCTTGCTGCATCCTCACCCCATCAGCATTATT
 -1756 CCCAGGGTAACTACTATTAATAGATAGTAATTCTACCCAAAGGAAAAATCATATGCATATAAC
 -1691 AGCATCATATGTATACCTTTCTAGTAACCTACAAAACAAATGATAATATCATATCCTTTCTTATG
 PvuII (-1580)
 -1626 TGTATTGCTCTTTTCACTAAATGTATCTGTGATATGTGTCTATATCAGCTGATTGTCCTTTTGA
 -1561 TGGCTGAATAATATTCATCTTGTCCACGTGATAGTATTACTTGACAAGCTCCCTGCTGATGGAC
 -1496 ATTTGCTTTGTTACTATGATAGTAATATAATCAACATTTATATATGTTTTGTATGTATCTATAA
 -1431 TACACATGCACATACACATGCATATTTCTGCAGGGATAGCCATAGTAAATAACTAGTAACGGTAT
 -1366 TGCAAGTTAAAGGAACAATCTCATTGCTTGAAATTTTAAATTTTGAAATACACTGCCAATTTTCA
 -1301 TGGTCTCTCCTTGTAAGCTAGTTTGGGCTTTCTCACAGCATGACAGGCTCAGGGCAGTCAGACCA
 -1236 TCCTGGCCAAAGAGCAGAGTGCCACAGACCACAACTGCTTCTAATCAGCCATCTTCCCAAAGCCT
 -1171 TCTCTTTTTTCTATTAATAACTTTGTATGAGATTCCATCTTAATACTTTTCTGTGTTTGGTCTT
 -1106 GTAAGAGCTTATTTTCTGAACCAGGAAGTGGTTCAGGGCGGTTTTCTAACTTCACAGAGCTCC
 -1041 CTCTTCTGTTAGCTTTTGTGAAATGGTCAAAAACATAGCAGCCTGCCTTCTGAGTTCTCCATCCC
 -976 ACCCTGGTTGGGCCTTCTCTATCCTTGTCTGTGTTGTTTATATCCTGCTGAAGTGTGATTCCACT

FIG. 14F

663070-6723600

-911 TGTGCAGTTTCTCCTCTGTGTAGGATCAAAGGGCTGTGGCTGGTTGGTTTGAAAATTTCTTATAC
-845 CCTAGACTATTCCAGTGCCTTTTCAAGGCTCTCACACTAATCTATTATCATATTG
-779 GGCAAACTCCTTGCAGTTTCAGCTACTATTCCTGATTGACTTTTCAGTAAATCTATCTCTCAGT
-713 CTTTCAGTATCCAAAGAAGATTGGTTCTAGGACCACCATCCCGCTGCCTCCACAGATACCAAAATC
-647 AGAGGATGCTCAATTCCTCTTATAAAACGTTGCAGTATTTGCATATAATCTGCACATGTATTTCT
-581 GTATATTTTAAATCATCCCTAGATTACTTATAATACCTGATACAATATAAATGCTAAATAGCTGTA
-515 ACACTGTATCTTTAAATTTACATTATTTTTTGTTGTTGTATTATTATTTTATGTATTTTTTAA
-449 AAATATTTTCCATCTACAGTCAGTAGAATCCACGGATACAGAACCTATGGATAGGAAGGACCAACT
-383 GTATCTTTTAGTGTTTTGAGGTTCTTG

FIG. 14G

-356 AATTCTCAGGTCGTTTGCTTTCTTTGCTTTCTCCCAAGTCTTGTTTTACAATTGCTTTAGTCA
-291 TTCACTGAAACTTTAAAAAACATTAGAAAACCTCACAGTTTGTAATCTTTTTCCCTATTATATA
-226 TATCATAAGATAGGAGCTTAAATAAAGAGTTTTAGAACTACTAAAATGTAAATGACATAGGAAA
-161 ACTGAAAGGGAGAAGTGAAAGTGGGAAATTCCTCTGAATAGAGAGAGGACCATCTCATATAAATA

CAP (-81)

-96 GGCCATACCCACGGAGAAAGGACATTCTAACTGCAACCTTTTCGAAGCCTTTGCTCTGGCACAACA

AUG (1)

-31 GGTAGTAGGGGACACTGTTCTGTTGTCAAC ATG ACC AAC AAG TGT CTC CTC CAA
25 ATT GCT CTC CTG TIG TGC TTC TCC ACT ACA GCT CTT TCC ATG AGC TAC
73 AAC TTG CTT GGA TTC CTA CAA AGA AGC AGC AAT TTT CAG TGT CAG AAG
121 CTC CTG TGG CAA TTG AAT GGG AGG CTT GAA TAC TGC CTC AAG GAC AGG

PvuII (199)

169 ATG AAC TTT GAC ATC CCT GAG GAG ATT AAG CAG CTG CAG CAG TTC CAG
217 AAG GAG GAC GCC GCA TTG ACC ATC TAT GAG ATG CTC CAG AAC ATC TTT
265 GCT ATT TTC AGA CAA GAT TCA TCT AGC ACT GGC TGG AAT GAG ACT ATT
313 GTT GAG AAC CTC CTG GCT AAT GTC TAT CAT CAG ATA AAC CAT CTG AAG
361 ACA GTC CTG GAA GAA AAA CTG GAG AAA GAA GAT TTC ACC AGG GGA AAA
409 CTC ATG AGC AGT CTG CAC CTG AAA AGA TAT TAT GGG AGG ATT CTG CAT
457 TAC CTG AAG GCC AAG GAG TAC AGT CAC TGT GCC TGG ACC ATA GTC AGA
505 GTG GAA ATC CTA AGG AAC TTT TAC TTC ATT AAC AGA CTT ACA GGT TAC

BglII (565)

553 CTC CGA AAC TGAAGATCTCCTAGCCTGTGCCTCTGGGACTGGACAATTGCTTCAAGCATTCT
615 TCAACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCATATGAAAGGACACTAGAAG

FIG. 15A

680 ATTTTGA AATTTTATTAAATTATGAGTTATTTTATTATTAAATTTTATTTTGAAAATAAA
745 TTATTTTGGTGCAAAGTCAACATGGCAGTTTAAATTCGATTTGATTTATATAACCATCCATA
810 TTATAAAATTGCCAAGTACCTATTAGTTGTTCTTTTAAAATATACCTGCAAAGTAGTATACTTT
875 CTGGCCCCTGCCTTTAAGGAATTTAAAATTCAAGAAAGCCATGATGGAATATATAAGGTAAGAGA
940 CAATAAGGGGACCTGAACCTTATGGGGGAATAAATATGGCATGAACTGCTGTGGGATTAAAAGAG
1005 AAAAGGAAAGCTGGAGGGTCTGGAATAAACCTGGGGTTCCTCCTCCTACTGTGTGTTCAG
Ball (1099)
1070 ATTCTCTCATCATAAAGTTAGAATTGAGCTGGCCATCAGGAATAGCCAGAGGAATATGTCAGCTT
1135 TTGTGTTCTCCCTAACCTTCCCCAGTTATTTGGGGGATCACTTTGCTCCTCGAAAGATTTTAA
1200 TAATTATGTGCCCCCACCATCCCTGCAA

FIG. 15B

680 745 810 875 940 1005 1070 1135 1200

Activation of the Human β -interferon Gene by Homologous Recombination with pINT β -1

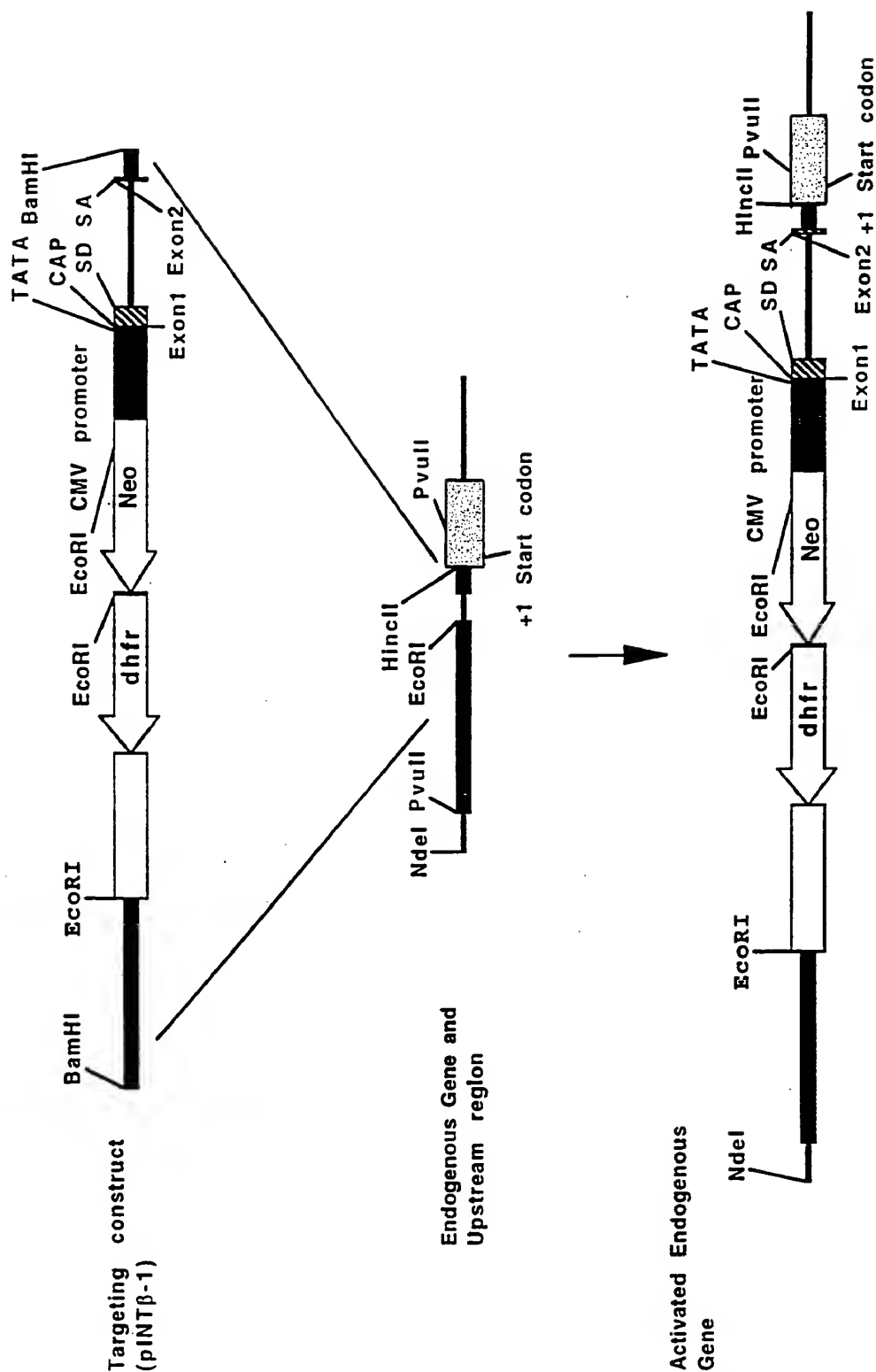


FIG. 16